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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/881,215

06/15/2001

Peter A. Crooks

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5136

7590

05/20/2004

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EXAMINER

KIM, VICKIE Y

ART UNIT

PAPER NUMBER

1614

DATE MAILED: 05/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/881,215	CROOKS ET AL.	
	Examiner	Art Unit	
	Vickie Kim	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on _____.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5,7,9,11 and 13-20 is/are pending in the application.
- 4a) Of the above claim(s) 1-4 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 5,7,9,11 and 13-20 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of Application

1. Acknowledgement is made of amendment filed 01/12/2004. Upon entering the amendment, the claims 5, 9, 11, 13 and 15-17 are amended and the claims 6, 8, 10 and 12 are canceled.
2. The claims 1-5, 7, 9, 11 and 13-20 are pending.
3. The elected claims 5, 7, 9, 11, 13-20 are presented for the examination and the non-elected claims 1-4 are maintained as withdrawn from consideration.

Response to Arguments

4. Applicant's arguments with respect to claims 5-20 have been considered but are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. Claims 5, 7, 9, 11, 13-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wada et al(1997).

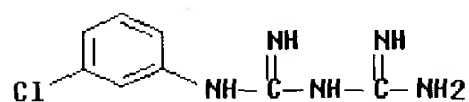
The claims are drawn to a method of treating, ameliorating, or preventing seizures associated with epilepsy in a subject in need thereof, the method comprising administering a pharmaceutical composition comprising about of 0.1-500mg of

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agmatine or agmatine analog having the formula recited in claim 5, or a pharmaceutically acceptable salt thereof per kilogram of the subject's weight.

Wada et al teach 1-(*m*-chlorophenyl)-biguanide and its therapeutic use in the treatment of seizures(i.e. reduction of the occurrence) associated with epilepsy, see abstract. Since 1-(*m*-chlorophenyl)-biguanide has the structure that is embraced by the generic formula of agmatine analog required by the claim 5, all the claimed subject matter is met by the teaching of cited reference and the claimed subject matter is not patentably distinct over the prior art of the record.

It is noted that 1-(*m*-chlorophenyl)-biguanide has the structure as following:



This compound is within the scope of the instant invention because it satisfy all the substitution suggested by the instant claims where the said agmatine analog of instant claims has the substitution of H on R2,R3,R4 and R5 independently, NH on Y, (C=N) on X and chloro-phenyl on R1 position.

Applicant's claims differ because they require specific dosage regimen(i.e. 0.1-500mg/kg) and the claims 13-20 require human subject.

However, it would have been obvious to one of ordinary skill in the art to modify Wada's teaching to incorporated into the human use at the time of the invention was made because it would have been most conventional medical practice to adapt the animal study into the human test where the techniques and skills for titrating the proper dosage regimen are well considered to be within the skilled level of the artisan having

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ordinary skills in the art, absent evidence to the contrary. Thus, all the claimed subject matter is not patentably distinct over the prior art of the record.

7. Claims 5, 7, 9, 11, 13-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Uzbay(2000) in view of Rajasekaran(2000).

Uzbay teaches agmatine(40mg) is effectively used in the treatment of audiogenic seizures due to ethanol withdrawal, see page 156. It further teaches that the therapeutic effects are resulted from blocking nitric oxide synthase and selective inhibition of the NMDA subclass of glutamate receptor channels.

Applicants' claims differ because they require seizures which is specifically caused by epilepsy and also differs because they require human subject.

Rajasekaran teaches an aticonvulsant activity of agmatine used in the treatment of seizure due to epilepsy, see pages 1st -5th. Rajasekaran further teaches the underlying mechanism for the anticonvulsant activity is utilizing NO inhibition wherein NO is produced in the neurons in response to activation by NMDA receptors , see 1st page.

Thus, it would have been obvious to one of ordinary skill in the art at the time of the invention was made to modify Uzbay's teaching in view of Rajasekaran to treat seizure caused by not only ethanol withdrawal but also seizure due to epilepsy. One would have been motivated to make such modification because seizure is the syndrome(symptom) which can be treated by same medication regardless of its own etiologies that could be different from one to the others because the medication corrects the underlying mechanism where the anticonvulsant action is mediated by.

One would have been motivated to do so, with reasonable expectation of success because it is always desirable to have extended therapeutic modalities to treat the diseases to improve the total quality of the care, especially when the drug is proven to be effective (corrects the underlying mechanism). The techniques and skills required for making such substitution is conventional knowledge or well within the skills of ordinary artisan, and thus obvious absent evidence to the contrary.

Conclusion

8. No claim is allowed.
9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

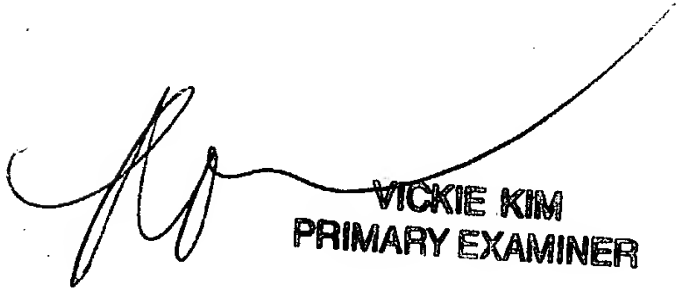
A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vickie Kim whose telephone number is 571-272-

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0579(fax: 571-273-0579). The examiner can normally be reached on Tuesday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel can be reached on 571-272-0584. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-746-3165 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.



VICKIE KIM
PRIMARY EXAMINER

Vickie Kim
May 17, 2004
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